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Reduction in Radiation Exposure in Cardiovascular CT Imaging

Results from the Prospective Multicenter Registry on Radiation Dose Estimates of Cardiac CT Angiography in Daily Practice in 2017 (*PROTECTION VI*)

Thomas J Stocker^{1,2}, Simon Deseive^{1,2}, Jonathon Leipsic³, Martin Hadamitzky⁴, Marcus Y Chen⁵, Ronen Rubinshtein⁶, Mathias Heckner¹, Jeroen J Bax⁷, Xiang-Ming Fang⁸, Erik Grove⁹, John Lesser¹⁰, Pál Maurovich-Horvat¹¹, James Otton¹², Sanghoon Shin¹³, Gianluca Pontone¹⁴, Hugo Marques¹⁵, Benjamin Chow¹⁶, Cesar H Nomura¹⁷, Ramzi Tabbalat¹⁸, Axel Schmermund¹⁹, Joon-Won Kang²⁰, Christopher Naoum²¹, Melany Atkins²², Eugenio Martuscelli²³, Steffen Massberg^{1,2} and Jörg Hausleiter^{1,2,*}, for the PROTECTION VI investigators[#]

¹ Medizinische Klinik und Poliklinik I, Ludwig Maximilians-Universität, Munich, Germany

² DZHK (German Center for Cardiovascular Research), Partner Site Munich Heart Alliance, Munich, Germany

³ University of British Columbia, Vancouver, Canada

⁴ Deutsches Herzzentrum, Munich, Germany

⁵ National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, United States

⁶ Lady Davis Carmel Medical Center, Haifa, Israel

⁷ Department of Cardiology, Leiden University Medical Center, Leiden, The Netherlands

⁸ Wuxi People's Hospital, Wuxi, China

⁹ Aarhus University Hospital, Aarhus, Denmark

¹⁰ Minneapolis Heart Institute at Abbott Northwestern Hospital, Minneapolis, United States

¹¹ Heart and Vascular Center, Budapest, Hungary

¹² Spectrum Radiology Liverpool, Sydney, Australia

¹³ National Health Insurance Service Ilsan Hospital, Goyang-si, South Korea

¹⁴ Centro Cardiologico Monzino, University of Milan, Milan, Italy

¹⁵ UNICA (cardiovascular CT and MRI Unit), Hospital da Luz, Lisboa, Portugal

¹⁶ University of Ottawa Heart Institute, Ottawa, Canada

¹⁷ Heart Institute - InCor, Sao Paulo, Brazil

¹⁸ Khalidi Hospital & Medical Center, Amman, Jordan

¹⁹ Cardioangiologisches Centrum Bethanien (CCB), Frankfurt, Germany

²⁰ Asan Medical Center, Seoul, South Korea

²¹ Macquarie University Hospital, Sydney, Australia

²² Fairfax Radiological Consultants, Fairfax, United States

²³ Policlinico di Tor Vergata, Rome, Italy

* Corresponding author. Tel: +49 89 4400 72361, Fax: +49 89 4400 78788, Email: joerg.hausleiter@med.uni-muenchen.de

All PROTECTION VI investigators are listed at the end of the manuscript

Abstract

Aims: Advances of cardiac CT angiography (CTA) have been developed for dose reduction, but their efficacy in clinical practice is largely unknown. This study was designed to evaluate radiation dose exposure and utilization of dose-saving strategies for contrast-enhanced cardiac CTA in daily practice.

Methods and Results: Sixty one hospitals from 32 countries prospectively enrolled 4502 patients undergoing cardiac CTA during one calendar month in 2017. CTA scan data and images were analyzed in a central core lab and compared to a similar dose survey performed in 2007. Linear regression analysis was performed to identify independent predictors associated with dose. The most frequent indication for cardiac CTA was the evaluation of coronary artery disease in 89% of patients. The median dose-length-product (DLP) of coronary CTA was 195 mGy*cm (IQR: 110 to 338 mGy*cm). When compared with 2007, the DLP was reduced by 78% ($p<0.001$) without an increase in non-diagnostic coronary CTAs (1.7% in 2007 vs. 1.9% in 2017 surveys, $p=0.55$). A 37-fold variability in median DLP was observed between the hospitals with lowest and highest DLP (range of median DLP: 57 to 2090 mGy*cm). Independent predictors for radiation dose of coronary CTA were: body weight, heart rate, sinus rhythm, tube voltage, iterative image reconstruction and the selection of scan protocols.

Conclusion: This large international radiation dose survey demonstrates considerable reduction of radiation exposure in coronary CTA during the last decade. However, the large inter-site variability in radiation exposure underlines the need for further site-specific training and adaptation of contemporary cardiac scan protocols.

Key words: Cardiac CT angiography, radiation dose exposure, dose-length-product, dose-saving strategies

Introduction

Cardiac computed tomography angiography (CTA) is an increasingly used noninvasive imaging method in cardiology.^{1,2} Due to the high diagnostic accuracy, coronary CTA clarifies the diagnosis of angina in patients with suspected coronary artery disease (CAD) in addition to standard clinical care³ and coronary CTA is able to rule out CAD with high negative predictive value.⁴ The improved diagnostic capabilities may alter downstream testing and clinical care in a significant proportion of patients, which may reduce cardiac events.^{3, 5} Finally, coronary CTA carries significant prognostic information.⁶

Radiation exposure from cardiac CTA carries the potential risk of cancer induction in a dose-dependent manner.⁷ Accordingly, safety considerations of cardiac CTA are an ongoing concern and CT imager should aim to reduce radiation dose exposure to be “as low as reasonably achievable” (ALARA principle), while maintaining diagnostic image quality.⁸ One decade ago, the international dose survey PROTECTION I collected data from 1965 cardiac CT studies and evaluated the radiation exposure from cardiac CTA.⁹ Since then, advances in CT technology including new acquisition techniques and software algorithms, have been developed and societal guidelines as well as clinical studies have advocated for a consequent use of these techniques to lower radiation dose.¹⁰⁻¹⁵ However, the utilization and efficacy of modern techniques for radiation dose reduction in real-world clinical practice across the globe is currently unknown. Thus, the current dose survey was designed to investigate the radiation dose of cardiac CTA, the utilization and efficacy of established dose saving strategies and the potential for further radiation dose reduction in a real-world setting in 2017.

Methods

Study protocol

The study design of the 2017 dose survey, entitled Prospective Multicenter Registry on Radiation Dose Estimates of Cardiac CT Angiography IN Daily Practice in 2017 (PROTECTION VI), has been described previously.¹⁶ The dose survey is an international, industry-independent, multi-vendor, prospective, observational study. With the objective to garner a representative worldwide sampling, a total of 435 clinicians from 62 different countries were invited as identified by literature research and by membership of the Society of Cardiovascular Computed Tomography (SCCT). The study collaborators enrolled all consecutive patients undergoing cardiac CTAs during one month between March and December 2017. CT studies before transfemoral aortic valve replacements were excluded, due to necessity to image the entire aorta and the heterogeneity in acquisition protocols. Cardiac CTAs were carried out according to local standard of clinical care. Data was analyzed in a central core laboratory. Each study site consulted the responsible local ethics committee to evaluate the study protocol, which had to be approved prior to patient enrollment. All patients gave written informed consent as required at the individual study sites and data was obtained prospectively. An Executive Steering Committee composed of a group of physicians with expertise in cardiac CTA, clinical research and statistics supervised the study. The study has been registered with clinicaltrials.gov (NCT02996903).

Strategies for Reduction of Radiation Dose

The selection of strategies for radiation dose reduction was at the discretion of the local study investigators. The conventional retrospectively ECG-gated helical scan protocol is a robust scan technique, which is least radiation efficient. Prospectively ECG-triggered scan techniques, including the axial and high-pitch scan modes, deliver the radiation efficiently

only during a short fraction of the R-R interval and is recommended for patients with sinus rhythm and heart rates ≤ 65 beats/min.¹¹ Reducing the tube potential from the conventionally used 120 kVp to 100 kVp lowers radiation exposure without compromising diagnostic image quality and has been recommended for patients with a body-mass-index (BMI) ≤ 30 kg/sqm.¹² The combination of iterative image reconstruction (IR) with reduced radiation tube currents has also been shown to reduce radiation exposure during coronary CTA without compromising diagnostic image quality.¹⁰

Estimation of radiation dose

The parameters relevant to radiation dose were obtained from the dose report generated by the CT system after each cardiac CTA study. The total dose-length-product (DLP), which includes the radiation exposure of the entire CT investigation including among others the localizer and timing bolus, was the main outcome measure. The DLP_{CTA} represents the radiation exposure, which was delivered for the acquisition of the CT angiography only. The DLP equals the CT dose index (CTDI_{vol}) multiplied by the respective scan length.

Image Quality

Diagnostic image quality of coronary CTAs was assessed by the local investigators. Non-diagnostic image quality was defined by severe vessel blurring or vessel discontinuity secondary to reconstruction artifacts, which did not allow the exclusion of obstructive coronary lesions. Coronary CTAs were considered as non-diagnostic when at least one coronary artery was of non-diagnostic image quality.

Statistical Analysis

Variables are expressed as counts with percentages or medians with interquartile ranges. Comparison of groups was performed with Wilcoxon-Mann-Whitney U-test or chi-square test as appropriate. Multivariable linear regression analysis with backward variable elimination was performed to identify predictors significantly associated with radiation dose in coronary CTA. A logistic regression analysis with the endpoint of performance to a diagnostic reference level was additionally performed. A generalized estimation equation model was used to account for the clustering effect of this multicenter trial. A p-value <0.05 was considered to be statistical significant. Statistical analysis was performed using R version 3.4.1.

Results

Patient and Study Site Characteristics

Clinicians of 61 international sites (42 university hospitals, 19 community hospitals) from 32 different countries participated in the study (see supplementary **Table S1** for regional enrollment). These sites contributed 4502 patients undergoing diagnostic cardiac CTA (median of 51 patients per site during the month of enrollment; IQR 27 – 91 patients). The median site experience for the performance of cardiac CTA studies was 10.5 years (IQR 7 – 13 years). Patient and study site characteristics of the 2017 dose survey are listed in **Table 1**; the characteristics of the 2007 dose survey are listed for comparison. In 2017, median patient's age was 60 years (IQR 51 - 69 years) and their median BMI was 26.8 kg/sqm (IQR 24.1 – 30.1 kg/sqm). Ninety percent of patients (4055 patients) were examined in sinus rhythm and beta blockers were administered in 66% (2973 patients) resulting in a median heart rate of 60 beats/min (IQR 55 – 67 beats/min).

The main indication for cardiac CTA was the evaluation of the coronary arteries (coronary CTA) in 89% of patients. Planning of electrophysiologic procedures (4%) and visualization of bypass grafts (3%) were less frequent indications. All four major CT manufacturers were represented with examination of at least 13% of the enrolled patients. At the time of data collection modern CT scanners were used in both surveys with 96% and 91% of scans performed 64-slice and ≥ 128 -slice CT scanners in the 2007 and 2017 dose surveys, respectively.

Radiation Dose

The median total DLP of all 4502 patients included in the 2017 dose survey was 252 mGy*cm (IQR 154 – 412 mGy*cm). The median total DLP for coronary CTAs was 246 mGy*cm (IQR 153 – 402 mGy*cm) with 79% of the radiation exposure resulting from the

coronary CTA (DLP_{CTA} : 195 mGy*cm, IQR 110 – 338 mGy*cm, **Table 2**). The observed DLP of 195 mGy*cm corresponds to effective doses of 2.7 or 5.1 mSv, estimated using the thoracic or the recently published cardiac DLP to effective dose conversion factor of 0.014 or 0.026 mSv / mGy*cm, respectively.^{17, 18} Compared with the 2007 survey, a significant 78% reduction in DLP_{CTA} was observed in 2017 ($p < 0.001$). The regional development of radiation exposure from 2007 to 2017 is presented in **Table 2**. **Figure 1** summarizes the reduction in radiation dose and the variability of DLP_{CTA} between study sites in the 2007 and 2017 dose surveys. While a 7-fold difference was observed in the 2007 dose survey between the study sites with lowest and highest median DLP_{CTA} (lowest and highest DLP_{CTA} in 2007: 331 and 2146 mGy*cm, respectively), this dose variability increased to a 37-fold difference in the 2017 dose survey (lowest and highest median DLP_{CTA} in 2017: 57 and 2090 mGy*cm, respectively). DLP_{CTA} data stratified for gender and CT manufacturer are displayed in **Figure 2** (further stratification according to CT model is given in supplementary **Figure S1**).

Compared to the 2007 dose survey, the reduction in radiation dose did not increase the rate of non-diagnostic CTA studies in 2017. The rates of non-diagnostic coronary CTAs were 1.7% and 1.9% in 2007 and 2017, respectively ($p = 0.55$).

Use of Dose Saving Strategies

The relationship between radiation tube potential and DLP_{CTA} is displayed in **Figure 3A**. Considering the cohorts of both surveys, the use of a tube potential of ≤ 100 kVp increased significantly from 5% to 56% in the 2007 and 2017 surveys. When a BMI threshold of ≤ 30 kg/sqm is considered for the eligibility of a ≤ 100 kVp tube potential, 6% and 70% of eligible patients were studied with a ≤ 100 kVp scan protocol in the 2007 and 2017 dose surveys, respectively. A tube potential of less than 100 kVp, which has not been used in 2007, was applied in 14% of patients in 2017.

In the 2007 dose survey, 94% of patients were scanned using retrospectively ECG-gated helical imaging and only 6% of patients were examined by prospectively ECG-triggered axial imaging. In the 2017 dose survey, retrospective helical imaging was decreasingly utilized in only 11% of patients and prospectively ECG-triggered axial scanning was favored in 78% of patients. ECG-triggered high-pitch helical imaging which is available on dual-source CT systems, was applied in 11%. Compared to retrospectively ECG-gated helical scanning, the prospectively ECG-triggered scan modes (axial or high-pitch) resulted in a 74% reduction in radiation dose in the 2017 dose survey ($p<0.001$; **Figure 3B**). IR methods, which were not available in 2007, were used in 83% of patients in the 2017. Application of IR techniques resulted in a 33% reduction of radiation dose, when compared with standard filtered back projection ($p<0.001$, **Figure 3C**).

Predictors for Radiation Dose

In the multivariable linear regression model, three patient-related and three scan-related variables of a total of 11 included parameters (see supplementary **Table S2**) were identified as independent predictors associated with radiation dose of coronary CTA. An increase in body weight of 10 kg, an increase in heart rate of 10 bpm and the absence of sinus rhythm were associated with an increase of radiation dose of 7%, 8% and 21%, respectively (all $p<0.01$; **Figure 4**). A decrease in the tube potential of 10 kVp and the use of IR were associated with a dose reduction of 21% and 30%, respectively (both $p<0.01$). Finally, the use of the ECG-gated low-pitch helical scan technique resulted in an increase of radiation dose by 313% ($p<0.001$), while the use of the ECG-triggered high-pitch scan technique was associated with 30% dose reduction ($p=0.08$) when compared to the axial scan technique. The results were confirmed in a second logistic regression model, which addressed the performance to the proposed diagnostic reference level (see also **discussion** and supplementary **Table S3**).

Discussion

Cardiovascular CT has become an established and increasingly used technique mainly for the diagnostic assessment of coronary artery disease burden in patients with chest pain. Although several studies have evaluated strategies to reduce the radiation exposure of cardiac CT imaging, there is still concern about the delivered dose in daily practice. The current international dose survey demonstrates that the radiation exposure associated with cardiovascular CT has been tremendously reduced by 78% over the last decade. This progress contributed to the establishment of cardiac CT as frequently used non-invasive imaging method supported by national guidelines.¹⁹ The determined international median DLP of coronary CTA corresponds to a recent national dose survey performed in the United Kingdom.²⁰ The achieved dose reduction can be attributed to several important factors: (1) the increasing awareness about radiation safety and the growing experience and knowledge of CT imagers in cardiovascular CT, (2) the publication and adherence to best practice guidelines for cardiac CT imaging,¹³ and (3) the availability of scan protocols in modern CT scanners, which are radiation dose efficient.

Scan protocols with a reduced tube potential and prospectively ECG-triggered scan protocols were, among others, the main contributor to the reduced radiation exposure in the 2017 dose survey. The use of 100 kVp instead of the conventional 120 kVp scan protocols in non-obese patients has been shown to reduce radiation exposure by 29% in a randomized comparison without compromising diagnostic image quality.¹² Over the last decade, the frequency of use of ≤ 100 kVp scan protocols has raised by over 10-fold from 5% in 2007 to 56% in 2017. Similarly, the use of prospectively ECG-triggered scan modes has shown to reduce radiation exposure by at least 69% without compromising diagnostic image quality.^{11, 21} These prospectively triggered scan modes were applied in 89% of patients undergoing coronary CTA in 2017, while the frequency was only 6% in 2007.

The observed low median DLP_{CTA} of 195 mGy*cm for a coronary CTA corresponds to an effective dose estimate of 2.7 or 5.1 mSv depending on the applied conversion factor ($k = 0.014$ or 0.026 mSv / mGy*cm)^{17, 18}. The effective dose estimates of coronary CTA are considerably lower than the recently published median effective dose estimates of 10.0 mSv for myocardial perfusion imaging, obtained from a comparable worldwide dose survey.²² This difference may result in an improvement in population safety, if coronary CTA would be preferably used over myocardial perfusion imaging in patients with suspected CAD. The current dose survey allow for the determination of a new diagnostic reference level for coronary CTA. The diagnostic reference level, which is typically set at the 75th percentile dose level for a typical-sized patient and for a certain radiological procedure, is not the recommended or preferred dose, but rather an action level at which additional investigation into the dose used should be performed. Based on the current results, a new diagnostic reference level of 400 mGy*cm should be considered for coronary CTA. In 2017, median DLPs for coronary CTA were above this proposed diagnostic reference level in 13 of 61 participating centers (see supplementary **Figure S2**). This observation but even more the 37-fold difference in median DLPs between the study sites with the lowest and highest median DLPs underlines the need and potential for further education around dose reduction strategies and standardization of coronary CTA scan protocols. Considering the 89% use of prospectively ECG-triggered scan protocols (axial or high-pitch) in the current survey, a further increase in use will be difficult to achieve, when the presence of a stable sinus rhythm and a heart rate of ≤ 65 beats/min are respected as selection criteria. In contrast, a scan protocol with ≤ 100 kVp tube potential was selected in “only” 70% of eligible patients, if a conservative BMI threshold of ≤ 30 kg/sqm was considered as eligibility criterion. Although this rate increased considerably from 2007 to 2017, this also indicates, that another 30% of patients with a BMI of ≤ 30 kg/sqm would have qualified for this dose saving scan protocol. A tube potential of 100 kVp has been successfully applied in some studies in patients up to a

body weight of even 100 kg without compromising image quality.²³ If this body weight threshold would have been exploited as eligibility criterion, then even 36% of patients from the 2017 dose survey would have qualified for a low-dose 100 kVp scan protocol. Finally, scan protocols with tube potentials less than 100 kVp have demonstrated a large potential for further dose reductions,²⁴ but they have been used only in 14% of patients in the current dose survey.

The results of the 2017 dose survey for cardiovascular CT have relevant implications on different levels of our health systems: On a **patient level**, the radiation doses should not discourage patients from undergoing coronary CTAs, when clinically indicated. In fact, an effective dose of 5 mSv in a 60-year-old patient (median age in the current survey) adds only a small, negligible additional risk to life-time cancer risk, but the diagnostic information and the clinical consequences resulting from a coronary CTA may outweigh this very small theoretical additional cancer risk. This becomes even more evident when the 0.05% estimated risk of fatal malignancy from a 10 mSv CT scan is compared to the 50% reduction in fatal and nonfatal myocardial reduction observed already 3 years after a coronary CTA.^{5, 25} However, the large variability in radiation doses between participating study sites indicates that patients may select certified non-invasive imaging centers for their CT studies, because the likelihood of obtaining low-dose CT studies might be higher in certified than non-certified imaging centers. On a **physician and institutional level**, a continuous monitoring of patient's radiation exposure as well as the participation in dose surveys^{20, 26} will allow for benchmarking with other physicians and institutions. The participation in such programs has been shown to improve "best practice" performance.²⁶ On a **societal level**, the 2017 radiation survey reveals the importance of education. The publication of guidelines as well as the organization of educational sessions on radiation exposure will improve the adherence to best practice recommendations.²⁷ Finally, on an **industry level**, the current study results claim for the set-up of default scan protocols, which are dose-efficient, as well as the development of

applications supporting the automated selection of optimal low-dose scan parameters, which will secure low-dose cardiac imaging for the individual patient.

Limitations

The lack of financial support for study conduction allowed the gathering of data without bias, but limited also the participation of additional sites.

In conclusion, the 2017 radiation dose survey demonstrates that the radiation exposure from cardiac CTA has been considerably reduced over the last 10 years. This was accomplished by an increased use of (a) low tube potential scan protocols, (b) prospectively ECG-triggered axial and high-pitch scan protocols, and (c) iterative image reconstruction. However, a large 37-fold inter-site variability in median radiation dose was observed, which underlines the need for further site-specific training and adaptation of contemporary cardiac scan protocols.

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Conflict of Interest: T.J. Stocker, S. Deseive, M. Hadamitzky, R. Rubinshtein, M. Heckner, J.J. Bax, X. Fang, E. Grove, J. Lesser, P. Maurovich-Horvat, J. Otton, S. Shin, G. Pontone, H. Marques, C. Nomura, R. Tabbalat, A. Schmermund, J. Kang, C. Naoum, M. Atkins, E. Martuscelli and S. Massberg report no relevant disclosures. J. Hausleiter reports research support and speaker honoraria from Abbott Vascular and Edwards LifeSciences, J. Leipsic reports personal fees from Heartflow and Circl CVI outside the submitted work, M. Chen reports non-financial support from Canon Medical systems outside the submitted work, B. Chow reports non-financial support from TeraRecon, grants from Ausculsciences and grants from CV Diagnostix during the conduct of the study.

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Figure legends

Figure 1: Reduction of dose-length-product from coronary CTAs and variation between study sites. Left: Box plots illustrate DLP of all coronary CTAs. Right: Variability of median DLP (\pm interquartile range, IQR) in the 2007 and 2017 dose surveys, respectively.

Figure 2: Differences in dose-length-product of coronary CTA by gender (A) and CT manufacturer (B).

Figure 3: Effect of dose saving strategies with tube potential reduction (A), scan mode (B) and application of IR (C) on dose-length-product in coronary CTA.

Figure 4: Independent predictors of radiation dose from coronary CTAs. Change of radiation dose in coronary CTA by independent patient and scan-associated factors as identified by a multivariable linear regression analysis. Retrospectively ECG-gated low-pitch helical and prospectively ECG-triggered high-pitch helical scan modes were compared to the axial scan technique.

Table 1: Patient and study site characteristics

	2007 Dose Survey (1965 patients)	2017 Dose Survey (4502 patients)
<i>Patient characteristics</i>		
Age, years	NA	60 (51 – 69)
Gender: male, %(n)	NA	58 (2623)
Patient height, m	1.70 (1.63 – 1.77)	1.70 (1.60 – 1.80)
Patient weight, kg	77 (66 – 87)	78 (67 – 90)
BMI, kg/sqm	26.2 (23.8 – 28.8)	26.8 (24.1 – 30.1)
Indication for cardiac CTA		
Coronary artery evaluation, %(n)	82 (1611)	89 (4006)
EP planning study, %(n)	2 (38)	4 (177)
CABG, %(n)	12 (225)	3 (122)
Other, %(n) ^a	4 (91)	4 (197)
β-Blocker medication		
None, %(n)	42 (828)	33 (1501)
Taking daily, %(n)	12 (233)	13 (603)
Administration for CTA, %(n)	46 (904)	53 (2370)
unknown, %(n)	0	0.6 (28)
Sinus rhythm, %(n)	95 (1874)	90 (4055)
Heart rate, beats/min	61 (55 – 75)	60 (55 – 67)
<i>Study site characteristics</i>		
Site experience, years	3 (1.5 – 5.5)	10.5 (7.0 – 13.0)
Number of cardiac CTAs/month	26 (10 – 46)	51 (27 – 93)
CT system		
16-slice CT, %(n)	4% (72)	0%
64-slice CT, %(n)	96% (1893)	9% (387)
≥128-slice CT, %(n)	NA	91% (4115)
CT manufacturer		
GE, %(n)	24 (466)	26 (1168)
Philips, %(n)	8 (159)	13 (574)
Siemens, %(n)	59 (1155)	48 (2160)
Toshiba, %(n)	9 (185)	13 (600)

Values are median (interquartile range) or % (number of patients). NA, not available.

^a Other indications for cardiac CTA included among others triple-rule-out CTs, visualization of the cardiac anatomy and coronary anomalies.

Table 2: Scan characteristics for coronary CT angiographies

	2007 Dose Survey (1611 patients)	2017 Dose Survey (4006 patients)	<i>P</i> value
Scan length, mm	131 (118 – 144)	137 (125 – 157)	< .001
Total DLP, mGy*cm	NA	246 (153 – 402)	NA
CTDI _{vol} _{CTA} , mGy	54 (38 – 74)	14 (8 – 24)	< .001
DLP _{CTA} , mGy*cm	885 (560 – 1239)	195 (110 – 338)	< .001
<i>Regional DLP for coronary CTA only</i>			
Europe, mGy*cm	814 (537 – 1151)	176 (93 – 312)	< .001
North America, mGy*cm	993 (292 – 1343)	199 (124 – 340)	< .001
Latin & South America, mGy*cm	1556 (711 – 1932)	295 (189 – 624)	< .001
Middle East, mGy*cm	1799 (1482 – 2138)	244 (132 – 400)	< .001
East Asia & Australia, mGy*cm	940 (599 – 1130)	169 (96 – 276)	< .001
<i>Dose Saving Strategies</i>			
Tube potential ≤100kV, %(n)	5 (82)	56 (2226)	< .001
Tube potential <100 kV, %(n)	0 (0)	14 (564)	NA
Retrospectively ECG-gated helical scan protocol, %(n)	94 (1512)	11 (447)	< .001
Subgroup with ECG-correlated modulation of tube current, %(n)	95 (1440)	73 (325)	< .001
Prospectively ECG-triggered axial scan protocol, %(n)	6 (99)	78 (3094)	< .001
Prospectively ECG-triggered high-pitch helical scan protocol, %(n)	0 (0)	11 (449)	NA
Iterative image reconstruction, %(n)	0 (0)	83 (3306)	NA
Values are median (interquartile range) or % (number of patients). NA, not available.			

Appendix

PROTECTION VI Investigators (sorted by country)

1. Patricia Carrascosa and Alejandro Deviggiano, Diagnóstico Maipú, Buenos Aires, Argentina
2. Christopher Naoum and John Magnussen, Macquarie University Hospital, Sydney, Australia
3. James Otton and Anthony Kaplan, Spectrum Radiology Liverpool, Sydney, Australia
4. Gudrun Feuchtner and Fabian Plank, Medizinische Universität, Innsbruck, Austria
5. Kristof De Smet and Nico Buls, Universitair Ziekenhuis, Brussel, Belgium
6. Roberto Caldeira Cury and Marcio Sommer Bittencourt, Delboni / DASA, Sao Paulo, Brazil
7. Cesar Higa Nomura and Roberto Nery Dantas Junior, Heart Institute – InCor, Sao Paulo, Brazil
8. Jonathon Leipsic and Philipp Blanke, University of British Columbia, Vancouver, Canada
9. Carl Chartrand-Lefebvre and Anne Chin, University of Montreal, Montreal, Canada
10. Gary Small and Benjamin Chow, University of Ottawa Heart Institute, Ottawa, Canada
11. Claudio Silva F, Clinica Alemana de Santiago, Santiago, Chile
12. Marcelo Godoy Z. and Claudio Silva F., Clinica Alemana de Temuco, Temuco, Chile
13. Xiang-Ming Fang and Wang Jie, Wuxi People's Hospital, Wuxi, China
14. Alberto Cadena, Clínica de la Costa, Barranquilla, Colombia
15. Theodor Adla and Vojtech Suchanek, Motol University Hospital, Prague, Czech Republic
16. Erik Lerkevang Grove and Kamilla Bech Pedersen, Aarhus University Hospital, Aarhus, Denmark
17. Jess Lambrechtsen and Mirza Husic, OUH-Svendborg, Svendborg, Denmark

18. Juhani Knuuti and Teemu Maaniitty, Turku University Hospital, Turku, Finland
19. Bernhard Bischoff and Elisabeth Arnoldi, Klinikum der Universität München, München, Germany
20. Axel Schmermund and Joachim Eckert, CCB, Frankfurt, Germany
21. Martin Hadamitzky and Tom Finck, Deutsches Herzzentrum München, München, Germany
22. Michaela Hell and Mohamed Marwan, Universitätsklinikum Erlangen-Nürnberg, Erlangen, Germany
23. Fabian Bamberg and Stefanie Mangold, Universitätsklinikum Tübingen, Tübingen, Germany
24. Thomas Schlosser and Johannes Ludwig, Universitätsklinikum Essen, Essen, Germany
25. Maria Mylona and Spyros Skiadopoulos, Olympion Hospital, Patras, Greece
26. Pál Maurovich-Horvat and Bálint Szilveszter, MTA-SE Cardiovascular Imaging Research Group, Heart and Vascular Center, Budapest, Hungary
27. Uday Jadav and Brian V. Pinto, MGM New Bombay Hospital, Vashi New Mumbai, India
28. Ronen Rubinshtein and Essam Hussein, Lady Davis Carmel Medical Center, Haifa, Israel
29. Daniele Andreini and Gianluca Pontone, Centro Cardiologico Monzino, Milan, Italy
30. Eugenio Martuscelli and Massimiliano Sperandio, Policlinico di Tor Vergata, Rome, Italy
31. Kakuya Kitagawa and Naoki Nagasawa, Mie University Hospital, Tsu, Japan
32. Ramzi Tabbalat and Rami A. Farhan, Khalidi Hospital, Amman, Jordan
33. Lilia M. Sierra Galán and Leovigildo A. Delgado, American British Cowdray Medical Center Observatory Campus, Mexico City, Mexico

34. Lilia M. Sierra Galán and Marco A. Reza Orozco, American British Cowdray Medical Center Santa Fe Campus, Mexico City, Mexico
35. Francisco C. Castellón and Mariana D. Zamudio, Instituto Ignacio Chavez, Mexico City, Mexico
36. Andres Preciado-Anaya and Rafael P. Gómez, Hospital Siena, Leon, Mexico
37. Signe Helene Forsdahl and Grete Anita Hansen, University Hospital North Norway, Tromsø, Norway
38. Anne Günther and Joanna F. Kristiansen, Oslo University Hospital Rikshospitalet, Oslo, Norway
39. Edith Chavez Huapalla and Percy Teran Chavez, Complejo Hospitalario San-Pablo, Surco, Peru
40. Hugo Marques and Pedro de A. Goncalves, UNICA (cardiovascular CT and MRI Unit), Hospital da Luz, Lisbon, Portugal
41. Subramaniyan Ramanathan, Al Wakra Hospital, Doha, Qatar
42. Valentin Sinitsyn and Maria Glazkova, Federal Center of Medicine and Rehabilitation, Moscow, Russia
43. Rami Abazid and Osama A. Smettei, Prince Sultan Cardiac Center, Burydah, Saudi Arabia
44. Ahmed Dawood and Salama Hussain Omar, Dr Erfan and Bagedo Hospital, Jeddah, Saudi Arabia
45. Joon-Won Kang and Dong Hyun Yang, Asan Medical Center, Seoul, South Korea
46. Tae Hoon Kim and Chul Hwan Park, Gangnam Severance Hospital, Seoul, South Korea
47. Sanghoon Shin and Seok Jong Ryu, Ilsan Hospital, Goyang-si, South Korea
48. Jose R. Palomares and Hug Cuellar, Hospital Val d'Hebron, Barcelona, Spain
49. Jeroen J. Bax and Alexander van Rosendael, Leiden University Medical Center, Leiden, Netherlands

50. Michelle C. Williams, David Newby and Edwin J. R. van Beek, University of Edinburgh, Edinburgh, United Kingdom
51. Russell Bull and Kavin Jayawardhana, Royal Bournemouth Hospital, Bournemouth, United Kingdom
52. Patricia Dickson and Jennifer Espey, Capital Cardiology Associates, Albany, United States
53. John Lesser and B. Kelly Han, Minneapolis Heart Institute, Minneapolis, United States
54. Renée Bullock-Palmer, Deborah Heart and Lung Center, Browns Mills, United States
55. Mark Rabbat and Nancy Schoenecker, Loyola University Medical Center, Maywood, United States
56. Dustin M. Thomas and Rosco S. Gore, San Antonio Military Medical, San Antonio, United States
57. Melany Atkins, Fairfax Radiological Consultants, Fairfax, United States
58. Marcus Y. Chen and Sujata M. Shanbhag, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, United States
59. John Mahmarian, Houston Methodist Hospital, Houston, United States
60. Jeannie Yu, Long Beach VA Healthcare System, Long Beach, United States
61. Todd C. Villines and Binh Nguyen, Walter Reed National Military Medical Center, Bethesda, United States of America

One-sentence summary

The PROTECTION VI study shows a considerable reduction of radiation dose in coronary CT imaging by 78% during the last decade, but also demonstrates the need for further site-specific training and adaptation of contemporary cardiac scan protocols as indicated by a large inter-site variability in radiation exposure.

Take-home figure

Figure 1 of the manuscript

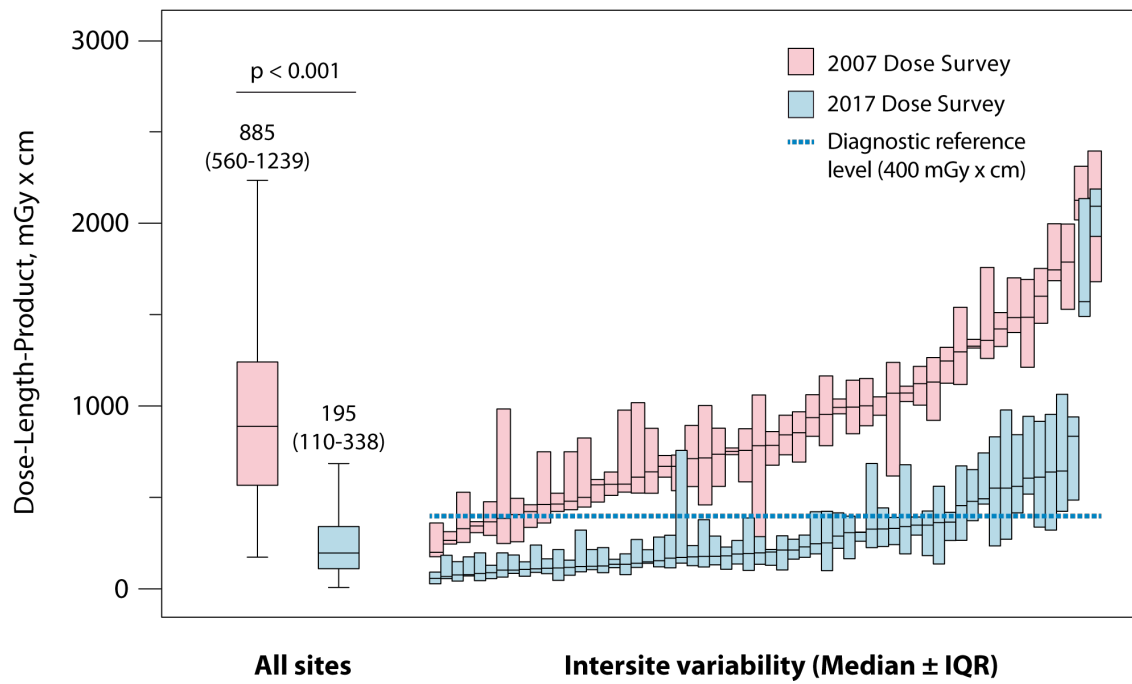


Figure 1

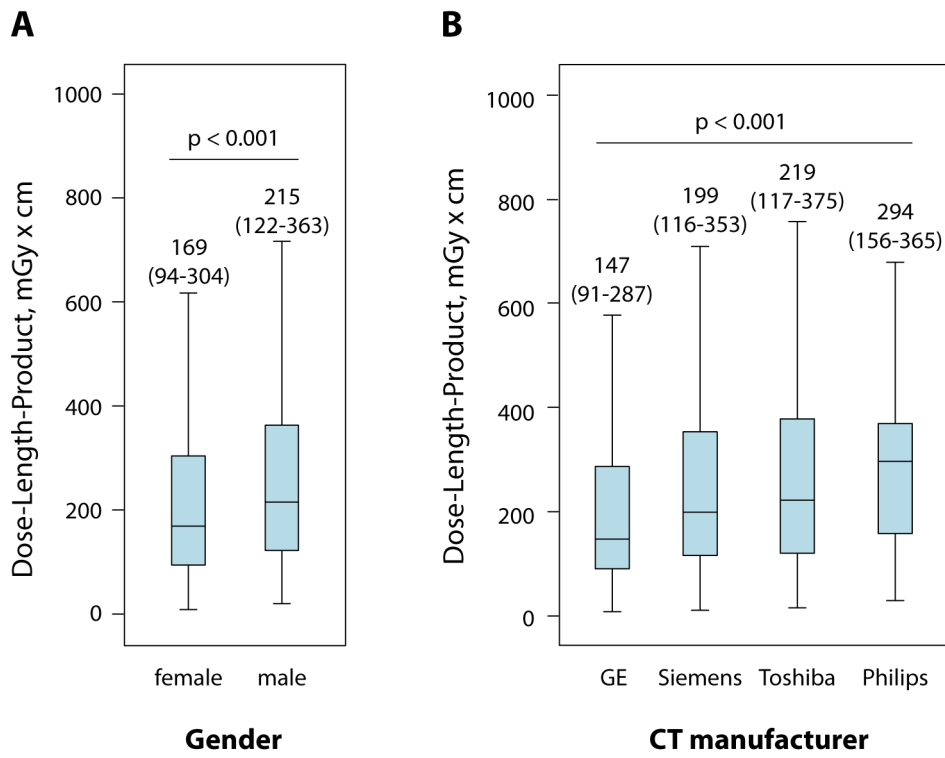


Figure 2

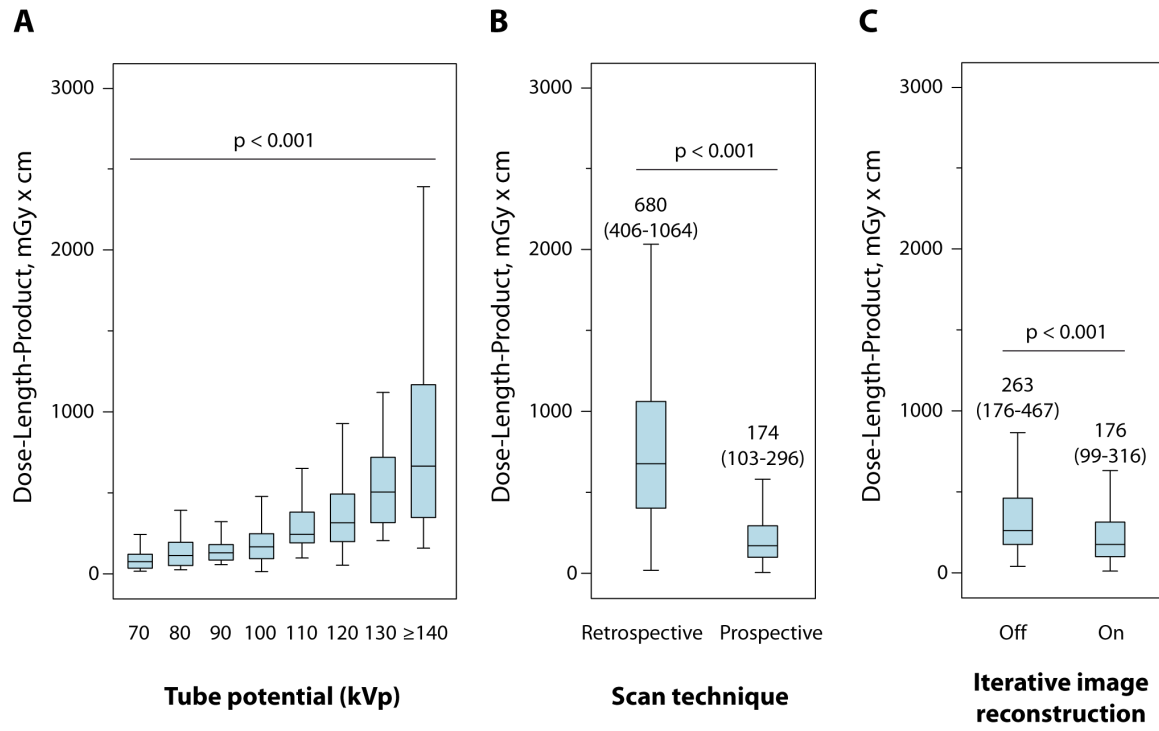


Figure 3

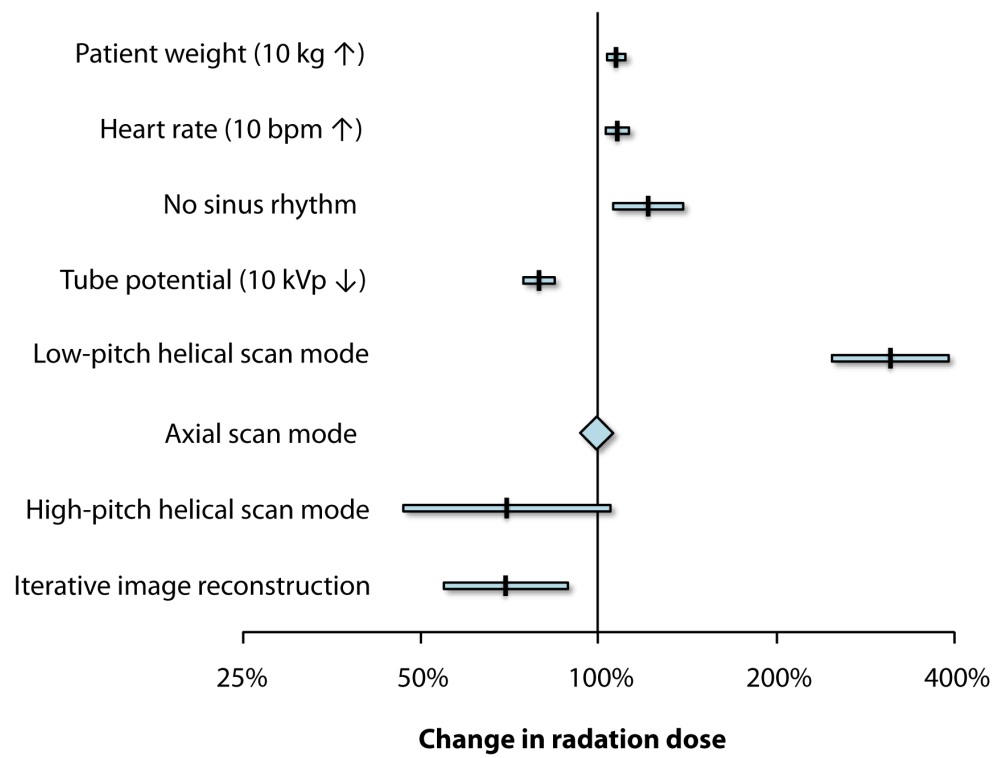


Figure 4